Interplay between membrane elasticity and active cytoskeleton forces regulates the aggregation dynamics of the immunological synapse

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Adhesion between a T cell and an antigen presenting cell is achieved by TCR–pMHC and LFA1–ICAM1 protein complexes. These segregate to form a special pattern, known as the immunological synapse (IS), consisting of a central quasi-circular domain of TCR–pMHC bonds surrounded by a peripheral domain of LFA1–ICAM1 complexes. Insights gained from imaging studies had led to the conclusion that the formation of the central adhesion domain in the IS is driven by active (ATP-driven) mechanisms. Recent studies, however, suggested that passive (thermodynamic) mechanisms may also play an important role in this process. In the talk, I will present our recent study of a simple lattice model which is capable of following the evolution of the system on length scales of several micrometers and time scales of minutes. The model takes into account the membrane-mediated thermodynamic attraction between the TCR–pMHC bonds and the effective forces that they experience due to ATP-driven actin retrograde flow and transport by dynein motor proteins. Monte Carlo simulations exhibit a very good spatio-temporal agreement with the experimentally observed pattern formation of the TCR–pMHC microclusters. The agreement is lost when one of the aggregation mechanisms is ‘‘muted’’, which helps to identify their respective roles in the process. We conclude that actin retrograde flow drives the centripetal motion of TCR–pMHC bonds, while the membrane-mediated interactions facilitate microcluster formation and growth. The interplay between the passive and active mechanisms regulates the rate of the accumulation process, which in the absence of one them proceeds either too quickly or slowly

[1] N. Dharan and O. Farago, Soft Matter **12**, 6649 (2016).

[2] N. Dharan and O. Farago, Soft Matter **13**, 6938 (2017).